April 30, 1958

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Dear Francois:

Esther and I are looking forward to seeing you again at Royaumont. We are very happy to accept your respective invitations. Our present plan is to arrive at Paris about Friday, July 26, so that we can visit with Bob Wright and Ephrussi at Gif before proceeding to the Abbey. We will advise you of our specific plans when they are settled.

Luca Cavalli and we are enjoying ourselves immensely in going over the interrupted mating experiments. I don't have to tell you what an elegant experimental advance this is, but it is so impressive in practice that I can hardly refrain. We are especially struck by the regularity with which the whole population conforms to the stated time of entry.

Unquestionably, if we were in your position we would have adopted the gradual entry of the Hfr chromosome into the F⁻ cell as a simple and compelling explanation. But you know the ambiguities which have been raised by our diploid results and we are still trying to reconcile the data in a single unassailable theory.

From a formal viewpoint at least we cannot make a critical decision between two material interpretations of "time of entry": (1) the time of first entry of the genetic material into the F⁻ cell, vs. (2) the time at which the parts of the preinjected nucleus enter into an effective pairing relationship with the homologous elements of the F⁻ chromosome. In order to sustain (2) a number of special assumptions are needed: a. that pairing starts at one point and proceeds progressively to, and sometimes beyond, a point of breakage (your R, our E), b. that all of the agencies which "interrupt mating pairs" also interfere with the internal pairing and c. that pairing is a prerequisite for zygotic induction and other phenodevelopmental processes. Of these assumptions (a) is equally as plausible as progressive entry; (c) is not offensive; but (b) puts a certain strain on the imagination. For the time being, therefore, (1) seems like the most useful working hypothesis, but we are reluctant to drop (2) for fear it may contribute an important element to the analysis, and in hopes of finding some way to definitely exclude it (or (1)). As you know I have never been hostile to the proposal of interrupted mating but felt that something had to be added to it, viz. a mechanism for <u>some</u> post zygotic eliminations. By recalling the formal ambiguity of "entry", i.e., entry into the cell or entry into synaptic relationship, we need no longer stumble over terminology for operational descriptions.

With regard to some other questions, I still feel that F is an extranuclear particle, perhaps analogous to the colicinogenic factors. Also that, while Hfr mutants often contribute to the futility of F^+ cultures, there is still an inherent futility of F^+. I am delighted that we can set a good example to some of our compatriots by being able to disagree vehemently on the best personal terms.

We have just one question to ask of the experimental operations: how do you plate a mating mixture without interrupting it? We found that spreading 0.05 ml samples on agar plates was as effective as blending, and had to flood the plates gently to avoid interruption.

I would also like to ask you some small favors: for 3 (additional?) reprints of your 1956 CSH paper; do you have any published details on inheritance of colicinogeny; have you studied zygotic induction with Hfr where Lp enters very early; what is the earliest time for any "ordinary" marker (i.e. one which is later with other Hfrs) among your various Hfrs?

With best regards,

JL/ew

encl.